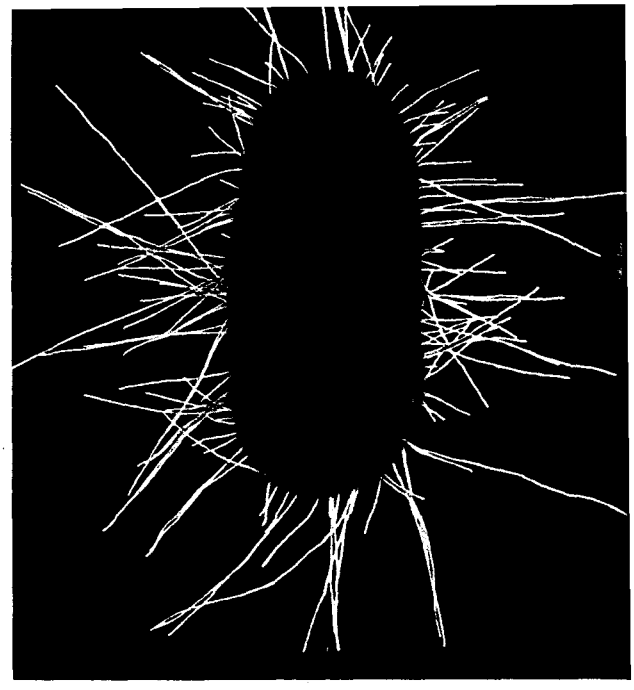
E. coli K-12

Joshua Lederberg



K-12 is possibly one of the most studied bacteria in science. Joshua Lederberg, whose pioneering work on bacterial genetics led to his winning the Nobel Prize in 1958, describes the fascinating history of this strain of *E. coli*.

TOP RIGHT:
Coloured transmission electron micrograph of a section through an *E. coli* K-12 bacterium.
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Theodor Escherich, a German pediatrician, cultured 'Bacterium coli' in 1885 from the faeces of healthy individuals, where it can be found almost universally in the large intestine, or colon, hence the 'coli'. It was renamed *Escherichia coli* in 1919 in a revision of bacteriological nomenclature, to lend more specificity to this particular form of Bacterium. From the beginning, although pathogenic strains were also found, *E. coli* was used as a representative, harmless bacterium that could be safely and easily cultivated even on synthetic media. On rich media, it will grow with a doubling time of 20 minutes; hence readily visible colonies can be seen overnight when it is plated on agar. Specialized media, like MacConkey's agar, were developed for the selective isolation and identification of *E. coli*, as this was used as a global indicator for the pollution of water supplies. Hence, during the first half of the 20th century, *E. coli* was well known to bacteriologists. However, it was rarely, if ever, mentioned in general biology texts, as bacteria were generally regarded as pre-cellular in complexity and devoid of the nuclei and other genetic apparatus of 'real' organisms.

The conceptual revolution that has catapulted bacteria into the spearhead of molecular genetic study dates to 1944. Avery, Macleod and McCarty reported that pneumococcal bacteria could be transformed in serological type with preparations of DNA, the first robust evidence that DNA had anything to do with genes. Unfortunately, there was little to connect that transformation with genes as known in higher organisms, and the opportunity to cross-breed bacteria and look for recombination and segregation in the style of Mendel was absent. Those challenges motivated my own work, which by 1946 filled that vacuum, with experiments on comprehensive genetic exchange and linkage mapping using *E. coli*.

E. coli was chosen for these studies because of its favourable husbandry just mentioned. Soon the Matthew Effect came into play: the very accumulation of knowledge, mostly concentrated on a single strain, 'K-12', made it more likely that it would be a prototype for still further studies. This strain was found to harbour a lysogenic bacteriophage, lambda, which has seeded a scientific industry of its own; it is also the seat of a number of plasmids – intracellular DNA particles transmitted by conjugation. The latter in turn provided the basis for gene-splicing, genetic engineering and modern biotechnology.

There are many myths about the provenance of 'K-12' – it has nothing to do with 'Kindergarten-12th Grade' primary education, which is the usual association with the acronym in the USA. Actually, strain K-12 was isolated at Stanford University in 1922 from human faeces, and was kept under that label for many years as a stock strain in the bacteriology department there. In the 1940s, Charles E. Clifton used it for studies of bacterial nitrogen metabolism, and his colleague Edward L. Tatum then borrowed it for his work on the biosynthesis of tryptophan from indole and serine. K-12 entered the domain of genetics with Tatum's pioneering studies on the production of nutritionally deficient mutants in 1944. That work led to my collaboration with Tatum, and the discovery of sexual recombination in 1946. Since then, K-12 has been used by thousands of other investigators for innumerable genetic studies, and its genome sequenced. In retrospect, we know how lucky was the choice of strain K-12. With the methods used in 1946, only one *E. coli* strain in twenty, chosen at random, would have been successfully crossed, owing to the idiosyncrasies of the F-plasmid which govern its sexual behaviour. Likewise, if it had carried prophages different from lambda, like P1, the integration of bacterial viruses into the chromosome might have been obscured.

During many years of cultivation in the laboratory, the strain has lost its 'O' surface antigens, which is just as well as it provides further assurance of its harmlessness to people. On the other hand, this has left K-12 out of the arena of study of pathogenesis, which comes to the fore with special strains of *E. coli* like O157, which betray close relationships to other pathogens like *Shigella*.

Some of the most important of the scientific applications of K-12 genetics have been in the field of gene regulation, and the elaboration of the concept of the 'operon', with work centred at the Pasteur Institute in Paris. The Nobel Prizes earned by Francois Jacob and Jacques Monod are but two of the dozen that by my account are affiliated with *E. coli*. The overall scientific literature alluding to *E. coli* now encompasses over 100,000 publications; Google reports almost 3 million hits with '*coli*' on the World Wide Web.

Further reading

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